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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/930,905	08/16/2001	Christopher Thomas Privalle	35780/238028 (5780-4)	1628

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EXAMINER

RUSSEL, JEFFREY E

ART UNIT PAPER NUMBER

1654

DATE MAILED: 09/26/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/930,905

Applicant(s)

PRIVALLE ET AL.

Examiner

Jeffrey E. Russel

Art Unit

1654

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 August 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11, 13-26, 28-30 and 32-35 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

- 5) ☒ Claim(s) 1-11, 13 and 15-21 is/are allowed.

- 6) ☒ Claim(s) 22-26, 28-30 and 32-35 is/are rejected.

- 7) ☒ Claim(s) 14 is/are objected to.

- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 16 January 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some * c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. _____.

3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9.

4) ☐ Interview Summary (PTO-413) Paper No(s). _____

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other:

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1. It should be noted that the dependencies of claims 6-9 were changed in the amendment filed August 5, 2003 without the changes being marked as required by 37 CFR 1.121. Any future amendments should be carefully checked to ensure compliance with the amendment rule.
2. Claim 28 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 28 is dependent upon canceled claim 27.
3. Claims 14 and 32-34 are objected to because of the following informalities: At claim 14, lines 2 and 3, "derivatives", "polyaldehydes", and "dextrans" should be changed to their singular form so as to match the indefinite article "a" which has been inserted into the claim. At claim 32, line 2, the word "a" (third occurrence) should be deleted. Appropriate correction is required.
4. Instant claims 1-35 are deemed to be entitled under 35 U.S.C. 119(e) to the benefit of the filing date of provisional application 60/253,758 because the provisional application, under the test of 35 U.S.C. 112, first paragraph, discloses the instant claimed invention.
5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
6. Claims 22-26, 28-30, and 32-35 are rejected under 35 U.S.C. 102(a) as being anticipated by the Privalle et al article (Free Radical Biology & Medicine, Vol. 28, pages 1507-1517). The Privalle et al article teaches pyridoxylated hemoglobin polyoxyethylene conjugate (PHP) which additionally comprises soluble red blood cell enzymes, including catalase and superoxide dismutase. The PHP is used in Phase II and Phase III clinical trials as a nitric oxide scavenger, e.g. in the treatment of septic shock. In general, hemoglobin-based therapeutics are described as being useful for blood replacement during surgery. See, e.g., the Abstract; page 1507; page

1514, paragraph bridging columns 1 and 2; and page 1515, column 1, last paragraph. Because the PHP compositions of the Privalle et al article are described as being used in Phase II and Phase III clinical trials, they are deemed inherently to be free of viral contamination to the same extent claimed by Applicants because the use of virally contaminated products is not permitted. Sufficient evidence of similarity is deemed to be present between the PHP of the Privalle et al article and the hemoglobin solution recited in Applicants' claims to shift the burden to Applicants to provide evidence that the hemoglobin solution recited in Applicants' claims is unobviously different than the PHP of the Privalle et al article. Note that even though the Privalle et al article does not teach or suggest a filtering method for producing its PHP, a novel and unobvious process of making a product does not necessarily result in a novel and unobvious product.

7. Claims 22-26, 28-30, and 32-35 are rejected under 35 U.S.C. 103(a) as being obvious over the Privalle et al article (Free Radical Biology & Medicine, Vol. 28, pages 1507-1517). Application of the Privalle et al article is the same as in the above rejection of claims 22-26, 28-30, and 32-35. To the extent that the Privalle et al article does not teach a hemoglobin solution of the same degree of purity as is recited in Applicants' claims, it would have been obvious to one of ordinary skill in the art at the time Applicant's invention was made to subject the PHP of the Privalle et al article to any known or combination of known purification procedures in order to reduce the viral contamination of the PHP, because it is known that blood products are susceptible to viral contamination, because it is desirable in the art to minimize viral contamination of all medical products in order to improve their safety, and because the use of known purification procedures in order to achieve only the expected purification is *prima facie*

obvious.

8. Claims 22-26, 28-30, and 32-35 are rejected under 35 U.S.C. 102(b) as being anticipated by the Privalle et al abstract (Free Radical Biology & Medicine, 6th Annual Meeting, Abstract No. 254). The Privalle et al abstract teaches pyridoxylated hemoglobin polyoxyethylene conjugate (PHP) which additionally comprises soluble red blood cell enzymes, including catalase and superoxide dismutase. The PHP is used in clinical trials as a nitric oxide scavenger, e.g. in the treatment of NO-induced shock characterized by hypotension. In general, hemoglobin-based therapeutics are described as being useful for blood replacement during surgery. Because the PHP compositions of the Privalle et al abstract are described as being used in clinical trials, they are deemed inherently to be free of viral contamination to the same extent claimed by Applicants because the use of virally contaminated products is not permitted. Sufficient evidence of similarity is deemed to be present between the PHP of the Privalle et al abstract and the hemoglobin solution recited in Applicants' claims to shift the burden to Applicants to provide evidence that the hemoglobin solution recited in Applicants' claims is unobviously different than the PHP of the Privalle et al abstract. Note that even though the Privalle et al abstract does not teach or suggest a filtering method for producing its PHP, a novel and unobvious process of making a product does not necessarily result in a novel and unobvious product.

9. Claims 22-26, 28-30, and 32-35 are rejected under 35 U.S.C. 103(a) as being obvious over the Privalle et al abstract (Free Radical Biology & Medicine, 6th Annual Meeting, Abstract No. 254). Application of the Privalle et al abstract is the same as in the above rejection of claims 22-26, 28-30, and 32-35. To the extent that the Privalle et al abstract does not teach a hemoglobin solution of the same degree of purity as is recited in Applicants' claims, it would

have been obvious to one of ordinary skill in the art at the time Applicant's invention was made to subject the PHP of the Privalle et al abstract to any known or combination of known purification procedures in order to reduce the viral contamination of the PHP, because it is known that blood products are susceptible to viral contamination, because it is desirable in the art to minimize viral contamination of all medical products in order to improve their safety, and because the use of known purification procedures in order to achieve only the expected purification is prima facie obvious.

10. Applicant's arguments filed August 5, 2003 have been fully considered but they are not persuasive.

The rejection based upon the Privalle et al article (Free Radical Biology & Medicine, Vol. 28, pages 1507-1517) is maintained. Applicants contend that the Privalle et al article does not enable one of ordinary skill in the art to make the PHP molecules used in the experiments reported in the reference. The examiner disagrees. The Privalle et al article teaches how to make the PHP molecules at page 1508, column 2, last two paragraphs, and page 1509, column 1, first three paragraphs, including the publications cited therein.

The rejection based upon the Privalle et al abstract (Free Radical Biology & Medicine, 6th Annual Meeting, Abstract No. 254) is maintained. Applicants contend that the Privalle et al abstract does not enable one of ordinary skill in the art to make the PHP molecules used in the experiments reported in the reference. The examiner disagrees. Prior art references are presumed operable and enabling, and the burden is on Applicants to provide evidence which rebuts this presumption. See MPEP 2121 and 2121.02. Applicants have not submitted any facts which would rebut the presumption. Further, the issue is not whether the reference enables itself,

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but rather whether the reference in combination with other prior art references known to one of ordinary skill in the art puts the public in possession of the claimed possession, i.e. provides an enabling disclosure of the portion of the reference relied upon in the rejection. See MPEP 2121.01. Accordingly, the prior art publications cited in Privalle et al article, page 1508, column 2, last two paragraphs, and page 1509, column 1, first three paragraphs, can be relied upon to show that the Privalle et al abstract is enabling, and any showing by Applicants of non-enablement would ultimately have to take into account and outweigh the evidence of enablement provided, e.g., by these prior art publications. Again, no factual showing of non-enablement has been submitted which would rebut the presumption of enablement afforded to the Privalle et al abstract.

The obviousness rejections based upon the Privalle et al article (Free Radical Biology & Medicine, Vol. 28, pages 1507-1517) and the Privalle et al abstract (Free Radical Biology & Medicine, 6th Annual Meeting, Abstract No. 254) are maintained. It is prima facie obvious to purify known products (see MPEP 2144.04(VII)), and in general one of ordinary skill in the art is capable of purifying known products. Applicants argue that prior art methods of viral decontamination would not permit production of a chemically modified hemoglobin which retains its endogenous antioxidant enzyme activity. If Applicants were to establish this by the submission of experimental evidence in an oath or declaration under 37 CFR 1.132, the examiner agrees that such a showing would rebut both obviousness rejections. However, the mere assertion is not sufficient to rebut the prima facie case of obviousness.

11. Claims 1-11, 13, and 15-21 are allowed. Claim 14 would be allowable if rewritten or amended to overcome the claim objection set forth in this Office action.

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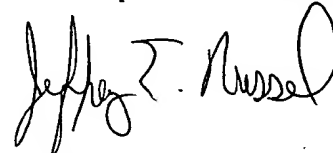
12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (703) 308-3975. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Brenda Brumback can be reached at (703) 306-3220. The fax number for Art Unit 1654 for formal communications is (703) 305-3014; for informal communications such as proposed amendments, the fax number (703) 746-5175 can be used. The telephone number for the Technology Center 1 receptionist is (703) 308-0196.



Jeffrey E. Russel
Primary Patent Examiner
Art Unit 1654

JRussel
September 24, 2003